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10/730,951	12/09/2003	Lee Dalton Jennings	AM100636	3667

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EXAMINER

COPPINS, JANET L

ART UNIT PAPER NUMBER

1626

DATE MAILED: 09/19/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

10/730,951

Applicant(s)

JENNINGS ET AL.

Examiner

Janet L. Coppins

Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 02 May 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-31 is/are pending in the application.
- 4a) Of the above claim(s) 19-31 is/are withdrawn from consideration.
- 5) ☒ Claim(s) 1-16 and 18 is/are allowed.
- 6) ☒ Claim(s) 17 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

1. Claims 1-31 are currently pending in the instant application.

#### ***Information Disclosure Statement***

2. Receipt is acknowledged of Applicants' Information Disclosure Statements (IDS), submitted March 5, 2004, September 6, 2004, November 10, 2005, and December 8, 2005, which have been considered by the Examiner. Please refer to the signed copies of Applicants' PTO-1449 forms submitted herewith.

#### ***Election/Restrictions***

3. The Markush group set forth in the claims includes both independent and distinct inventions, and patentably distinct compounds (or species) within each invention. However, this application discloses and claims a plurality of patentably distinct inventions far too numerous to list individually. Moreover, each of these inventions contains a plurality of patentably distinct compounds, also far too numerous to list individually. For these reasons provided below, restriction to one of the following inventions is required under 35 U.S.C. 121:

- I. Claims 1-16 and 18, drawn to compounds and compositions, classified in various subclasses of classes 546, 548, 549 and 514. A further election of a single disclosed species will be required if this Group is elected.
- II. Claim 17, drawn to a methods of using compounds according to claim 1 to inhibit plasminogen activator inhibitor in a mammal, classified in various subclasses of class 514. A further election of a single disclosed species will be required if this Group is elected.

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III. Claims 19-26, drawn to various methods of using compounds according to claim 1, for cardiovascular uses, classified in various subclasses of class 514. A further election of a single disclosed species will be required if this Group is elected.

IV. Claims 27-31, drawn to different methods of using compounds of claim 1, that are not for cardiovascular use, classified in various subclasses of class 514. A further election of a single disclosed species will be required if this Group is elected.

**In addition to an election of one of the above Groups, restriction is further required under 35 U.S.C. 121 as follows:**

4. In accordance with the decisions in *In re Harnisch*, 631 F.2d 716, 206 USPQ 300 (CCPA 1980); and *Ex parte Hozumi*, 3 USPQ2d 1059 (Bd. Pat. App. & Int. 1984), restriction of a Markush group is proper where the compounds within the group either (1) do not share a common utility, or (2) do not share a substantial structural feature disclosed as being essential to that utility. In addition, a Markush group may encompass a plurality of independent and distinct inventions where two or more members are so unrelated and diverse that a prior art reference anticipating the claim with respect to one of the members would not render the other members obvious under 35 U.S.C. 103.

5. Where an election of any one of Groups I-IV is made, an election of a single disclosed compound (in the specification) is further required, including an exact definition of each substituent on the base molecule (Formula I), wherein a **single member** at each substituent group or moiety is selected. For example, the base compound has the substituent group R<sub>2</sub>, wherein R<sub>2</sub> is recited to be any one of hydrogen, alkyl, cycloalkyl, thienyl, furanyl, oxazoyl, phenyl, etc., such that Applicant must select a single substituent for R<sub>2</sub>, for example hydrogen,

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and each subsequent variable position. In the instant case, the Office will review the claims and disclosure to determine the scope of the independent invention encompassing the elected compound (compounds which are so similar thereto as to be within the same inventive concept and reduction to practice). The scope of an independent invention will encompass all compounds within the scope for the claim which fall into the same class and subclass as the elected compound (or set of compounds). Examination will then proceed on the elected compound AND the entire scope of the invention encompassing the elected species, as defined by the above Groups and common classification. Should applicant traverse on the ground that the compounds are not patentable distinct, applicant should submit evidence now of record showing the compounds to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other.

All compounds falling outside the class(es) and subclass(es) of the selected compound and other compounds encompassed by the elected Group above will be directed to nonelected subject matter and will be withdrawn from consideration under 35 U.S.C. 121 and 37 C.F.R.

1.142(b). Applicant may reserve the right to file divisional applications on the remaining subject matter. (The provisions of 35 U.S.C. 121 apply with regard to double patenting covering divisional applications).

6. Applicant is reminded that upon cancellation of claims to a non-elected invention, the inventors must be amended in compliance with 37 CFR 1.48(b) if one of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any

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amendment of inventorship must be accompanied by a petition under 37 DFR 1.48)b) and by the fee required under 37 DFR 1.17)I).

7. Markush claims must be provided with support in the disclosure for each member of the Markush group. See MPEP 608.01(p). Applicant should exercise caution in making a selection of a single member for each substituent group on the base molecule to be consistent with the written description.

***Rationale Establishing Patentable Distinctiveness Within Each Group***

8. Each Group listed above is directed to or involves the use of compounds which are recognized in the art as being distinct from one another because of their diverse chemical structure, their different chemical properties, modes of action, different effects and reactive conditions (MPEP 806.04, MPEP 808.01). Additionally, the level of skill in the art is not such that one invention would be obvious over either of the other inventions (Groups), i.e. they are patentable over each other. Chemical structures that are similar are presumed to function similarly, whereas chemical that are not similar are not presumed to function similarly. The presumption even for similar chemical structures though is not irrefutable, but may be overcome by scientific reasoning or evidence showing that the structure of the prior art would not have been expected to function as the structure of the claimed invention. Note that in accordance with the holdings of **Applications of Papesch**, 50 CCPA 1084, 315 F.2d 381, 137 USPQ 43 (CCPA 1963) and **In re Lalu**, 223 USPQ 1257 (Fed. Cir, 1984), chemical structures are patentably distinct where the structures are either not structurally similar, or the prior art fails to suggest a function of a claimed compound would have been expected from a similar structure.

***The above Groups represent general areas wherein the inventions are independent and distinct, each from the other because of the following reasons:***

9. Invention I is related to Inventions II, III, and IV as product and processes of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, the process as claimed can be practiced with another materially different product since there are many known therapies for treating thrombosis and cardiovascular disease such as heparin, warfarin,  $\text{Ca}^+$  channel blockers, etc. Therefore separate search conditions are involved, which would impose a burden if unrestricted.
10. The Inventions of Group I are related as mutually exclusive species in the Markush group of formula (I). The species are distinct and independent from each other because the compounds differ structurally, one from the other as defined by the different variables recited in the claims. For example, within claim 1, the variable  $\text{R}_2$  alone has many separate, generic possibilities, including, for example, substituted carbon or heteroatoms which form distinct heterocyclic ring systems, which cannot be said to belong to the same class and subclass of chemical classification. Absent factual evidence to the contrary, each is a different chemical compound.
11. Because these inventions are distinct for the reasons given above and the search required for Group I is not required for Groups II-IV, restriction for examination purposes as indicated is proper.

***Advisory of a Rejoinder***

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12. The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and the product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise require all the limitations of the allowable product claim will be considered for rejoinder. All claims directed a nonelected process invention must require all the limitations of an allowable product claim for that process invention to be rejoined. Please refer to the following, a recitation of MPEP 821.04, Rejoinder:

Where product and process claims drawn to independent and distinct inventions are presented in the same application, applicant may be called upon under 35 U.S.C. 121 to elect claims to either the product or process. See MPEP § 806.05(f) and § 806.05(h). The claims to the nonelected invention will be withdrawn from further consideration under 37 CFR 1.142. See MPEP § 809.02(c) and § 821 through § 821.03. However, if applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims which depend from or otherwise include all the limitations of the allowable product claim will be rejoined.

Where the application as originally filed discloses the product and the process for making and/or using the product, and only claims directed to the product are presented for examination, when a product claim is found allowable, applicant may present claims directed to the process of making and/or using the patentable product by way of amendment pursuant to 37 CFR 1.121. In view of the rejoinder procedure, and in order to expedite prosecution, applicants are encouraged to present such process claims, preferably as dependent claims, in the application at an early stage of prosecution. Process claims which depend from or otherwise include all the limitations of the patentable product will be entered as a matter of right if the amendment is presented prior to final rejection or allowance. Amendments submitted after final rejection are governed by 37 CFR 1.116. Process claims which do not depend from or otherwise include the limitations of the patentable product will be withdrawn from consideration, via an election by original presentation (see MPEP § 821.03). Amendments submitted after allowance are governed by 37 CFR 1.312. Process claims which depend from or otherwise include all the limitations of an allowed product claim and which meet the requirements of 35 U.S.C. 101, 102, 103, and 112 may be entered.

Where product and process claims are presented in a single application and that application qualifies under the transitional restriction practice pursuant to 37 CFR 1.129(b), applicant may either: (A) elect the invention to be searched and examined and pay the fee set forth in 37 CFR 1.17(s) and have the additional inventions searched and examined under 37 CFR 1.129(b)(2); or (B) elect the invention to be searched and examined and not pay the additional fee (37 CFR 1.129(b)(3)). Where no additional fee is paid, if the elected invention is directed to the product and the claims directed to the product are subsequently found patentable, process claims which either depend from or include all the limitations of the allowable product will be rejoined. If applicant chooses to pay the fees to have the additional inventions searched and examined pursuant to 37 CFR 1.129(b)(2) even if the product is found allowable, applicant would not be entitled to a refund of the fees paid under 37 CFR 1.129(b) by arguing that the process claims could have been rejoined. 37 CFR 1.26(a) states that "[T]he Commissioner may refund any fee paid by mistake or in excess of that required. A change of purpose after the payment of a fee...will not entitle a party to a refund of such fee..." In this case, the fees paid under 37 CFR 1.129(b) were not paid by mistake nor paid in excess, therefore, applicant would not be entitled to a refund. In the event of rejoinder, the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. If the application containing the rejoined claims is not in condition for allowance, the subsequent Office action may be made final, or, if the application was already under final rejection, the next Office action may be an advisory action.



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13. The following is a recitation from paragraph five, "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai*, *In re Brouwer* and 35 U.S.C. 103(b)" (1184 TMOG 86(March 26, 1996)):

"However, in the case of an elected product claim, rejoinder will be permitted when a product claim is found allowable and the withdrawn process claim **depends from or otherwise includes all of the limitations of an allowed product claim**. Withdrawn process claims not commensurate in scope with an allowed product claim will not be rejoined." (emphasis added)

Therefore, in accordance with MPEP 821.04 and *In re Ochiai*, 71 F. 3d 1565, 37 USPQ 1127 (Fed. Cir. 1995), rejoinder of product claims with process claims commensurate in scope with the allowed product will occur following a finding that the product claims are allowable. Until, such time, a restriction between product claims and process claims is deemed proper.

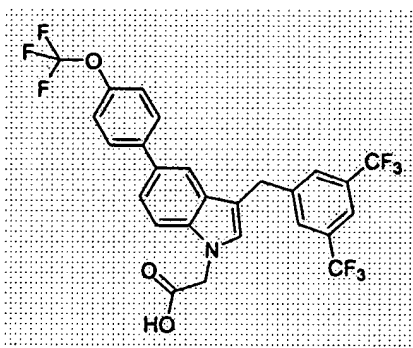
In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103 and 112. Until all claims to the elected product are found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained.

Withdrawn process claims that are not commensurate in scope with an allowable product claim will not be rejoined. See MPEP § 821.04(b). Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during prosecution to require the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

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***Telephonic Election***

14. During a telephone conversation with Wendy Choi, Reg. No. 36,697, a provisional election was made **with traverse** to prosecute the invention of Group I, claims 1-16 and 18, drawn to compounds and compositions. Affirmation of this election must be made by applicant in replying to this Office action. Claims 17 and 19-31 withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to non-elected inventions. Applicants further elect the compound of Example 2 in the Specification for examination (please refer to paragraph "5" above):



which is {3-[3,5-bis(trifluoromethyl)benzyl]-5-[4-(trifluoromethoxy)phenyl]-1H-indol-1-yl}acetic acid.

***Status of the Claims***

15. Claims 1-31 are pending in this application. Applicants have elected Group I with traverse, as well as the specific compound of Example 2 in the Specification. Claims 17 and 19-31 currently withdrawn from consideration as being drawn to non-elected inventions.

16. After a thorough examination of the compounds according to formula (I), claims 1-16 and 18 are directed to an allowable product. Pursuant to the procedures set forth in MPEP § 821.04(b) and *In re Ochiai*, see above, Group II, claim 17, directed to the process of using the

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allowable product, previously withdrawn from consideration as a result of a restriction requirement, is hereby rejoined and fully examined for patentability under 37 CFR 1.104. Claims 19-31, directed to the invention(s) of Groups III-IV, which require all the limitations of an allowable product claim, have NOT been rejoined.

Because a claimed invention previously withdrawn from consideration under 37 CFR 1.142 has been rejoined, **the restriction requirement between groups I and II as set forth in the instant Restriction, is hereby withdrawn.** In view of the withdrawal of the restriction requirement as to the rejoined inventions, applicant(s) are advised that if any claims including all the limitations of an allowable product claim or rejoined process claim are presented in a continuation or divisional application, such claims may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Once the restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. See *In re Ziegler*, 443 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

16. Applicant is reminded that upon the cancellation of subject matter to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

***Claim Rejections - 35 USC § 112***

17. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

18. Claim 17 rejected under 35 U.S.C. 112, first paragraph, as not being fully enabled. While various diseases/disorders related to the production of the serine protease inhibitor PAI-1 may be listed on pages 14-17 of the specification, the claims are not enabled for a blanket treatment method of “inhibiting PAI-1 in a mammal” since there is no indication as to the full range of diseases or disorders that could be treated using the instant claimed process.

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. § 112, first paragraph, have been described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

In the instant case, the claims are directed to many diseases and conditions that are not enabled in the specification, including those encompassed by the language of claim 17.

***The nature of the invention***

The nature of the invention is of methods of treating many different diseases or

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conditions that respond to the inhibition of PAI-1, comprising administering the instant claimed compound to a mammal in need thereof.

***The state of the prior art and the predictability or lack thereof in the art***

It is well recognized in the medical art that treatment of diseases or symptoms are not analogous terms. Furthermore, the diseases listed in the description on pages 14-17 of the specification are not the same but include different cancers as well as proliferative diseases such as psoriasis and cardiovascular diseases such as atherosclerosis. The nature of pharmaceutical arts is that it involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities. There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face. Also, in the absence of a showing of correlation between all the diseases claimed as capable of being treated by the compound of formula 1 and the inhibition of PAI-1, one of skill in the art is unable to fully predict possible results from the administration of the compound of formula 1.

***The amount of direction or guidance present and  
the presence or absence of working examples***

The applicable rule is that "Each claim must be separately analyzed and given its broadest reasonable interpretation in light of and consistent with the written description." MPEP 2163(II)(1), citing In re Morris, 127 F.3d 1048, 1053-1054; 44 USPQ2d 1023, 1027 (Fed. Cir. 1997). Applying this rule to claim 17, the scope of diseases claimed to be prevented or treated would thereby include all types of proliferative diseases, including psoriasis, Alzheimer's,

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nephropathy, neuropathy, retinopathy, diabetes, arthritis, and all types and kinds of cancer, including such diverse types of cancer as liposarcomas, epithelial tumors, breast cancer, ovarian cancer, etc., and all types of cardiovascular diseases including hypertension, atherosclerosis, venous and arterial thrombosis, coagulation syndromes, peripheral arterial disease, angina, etc. Furthermore, treatment of the claimed broad range of diseases are normally disease or symptom oriented, thus are highly individualized, i.e. treating each and every disease encompassed by the claimed “proliferative diseases” would not employ the same methods. The efficacy of an individual compound against a specific disease or symptom needs to be specifically and individually supported by factual evidence. Such evidence has not been described or supported by the specification.

The Specification only describes a few *in vitro* assays of PAI-1 inhibition, demonstrating concentrations of the claimed compounds of Formula (1) needed to suppress 50% suppression of cell proliferation ( $IC_{50}$  values), please see the Specification, pages 22-24. Given the scope of the many types of diseases/disorders included within the method claims, their varied etiologies, and the diversity of their patient populations, the disclosure in the Specification is insufficient to permit a person skilled in the art to practice a method for “inhibiting plasmogen activator inhibitor in a mammal” without naming any specific diseases of real-world relevance. While the Applicants cite specific diseases on pages 15-17 of the specification such as psoriasis, restenosis, and atherosclerosis, and cancers such as breast cancer and ovarian cancer and also provide many examples of how to prepare the instantly claimed compounds, there is no indication that the compounds can treat the entire scope of all named diseases. Applicants have provided evidence that the compounds are effective for treating murine colon tumors, however “the selection of the

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examples...used as the disclosure to support a claim must be adequately representative of the area covered by it," please see In re Cavallito et al. (CCPA 1970) 429 F.2d 452, 166 USPQ 552. Therefore the specification is enabled for certain proliferative diseases including psoriasis, restenosis, and atherosclerosis, and certain cardiovascular diseases, however the instant specification is lacking significant data to accommodate as many diseases as the claims are alleging by reciting the broad mechanism of "inhibiting PAI-1." The test of enablement is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. " In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) (citing In re Angstadt, 537 F.2d 489, 502-04, 190 USPQ 214, 217-19 (CCPA 1976)).

### ***The breadth of the claims***

As noted earlier, the applicable rule is that "Each claim must be separately analyzed and given its broadest reasonable interpretation in light of and consistent with the written description." In view of this rule, claim 17 may be reasonably interpreted to encompass atherosclerosis, vasculitis, nephritis, restenosis, arthritis, psoriasis, idiopathic pulmonary fibrosis, etc and forms of cancer and cancerous tumors, as neither the claims nor the Specification expressly define a closed set of illnesses. The scope of the claim reasonably encompasses such a broad spectrum of diseases/disorders that it is unreasonable to believe, on its face, that a particular chemical compound could be used for treating so many different types, in the absence of supporting scientific data or references in the disclosure to the contrary.

***The quantity of experimentation needed***

The quantity of experimentation needed is undue. One of ordinary skill in the art without direction, would be unable to treat each and every disease/condition encompassed by claim 17 using the instant claimed compounds. One of skill in the art would need to determine what proliferative diseases and cancers would be benefited by the inhibiting PAI-1 and would furthermore then have to determine whether the claimed compounds would provide treatment of all of the diseases and conditions by said activity.

***The level of the skill in the art***

The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by *in vitro* and *in vivo* screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Thus, the specification fails to provide sufficient support of the broad use of the compound of formula I for treating all diseases encompassed by the process of inhibiting PAI-1 in claim 17. As a result, necessitating one of skill to perform an exhaustive search for which claimed diseases can be treated by the compound of claim 1 in order to practice the claimed invention.

The Examiner suggests narrowing the scope of the diseases recited in claim 17, for example, "A method of inhibiting plasminogen activator inhibitor in a mammal for treating psoriasis, restenosis, atherosclerosis, stroke, hypertension, peripheral arterial disease, inflammation, coronary heart disease,..." etc.



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***Conclusion***

19. In conclusion, claims 1-31 are pending in the application. Claims 19-31 are currently withdrawn from consideration, and claim 17 stands rejected. Claims 1-16 and 18 appear allowable over the prior art.

***Telephone Inquiry***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Coppins whose telephone number is 571.272.0680. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph K. McKane can be reached on 571.272.0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

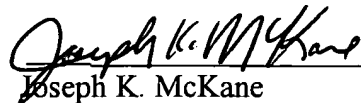
Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Janet L. Coppins  
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\_\_\_\_\_  
Joseph K. McKane  
SPE, Art Unit 1626